PATENT

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

- 1. (Currently amended) A phthalocyanine dye comprising a luminescent fluorophore moiety having at least one silicon containing [[an]] aqueous-solubilizing moiety, wherein said phthalocyanine dye has a core atom selected from the group consisting of Si, Ge, Sn, and Al; wherein said phthalocyanine dye exists as a single core isomer, essentially free of other isomers; and has a reactive or activatible group.
- 2. (Original) The phthalocyanine dye of claim 1, wherein said core atom is Si.
- 3. (Original) The phthalocyanine dye of claim 2, wherein said dye has Formula I:

I

wherein:

R is a member selected from the group consisting of -L-Q and -L-Z¹;

PATENT

L is a member selected from the group consisting of a direct link, or a covalent linkage, wherein said covalent linkage is linear or branched, cyclic or heterocyclic, saturated or unsaturated, having 1-60 atoms selected from the group consisting of C, N, P, O, and S, wherein L can have additional hydrogen atoms to fill valences, and wherein said linkage contains any combination of ether, thioether, amine, ester, carbamate, urea, thiourea, oxy or amide bonds; or single, double, triple or aromatic carbon-carbon bonds; or phosphorus-oxygen, phosphorus-sulfur, nitrogen-nitrogen, nitrogen-oxygen, or nitrogen-platinum bonds; or aromatic or heteroaromatic bonds;

Q is a reactive or an activatible group;

 Z^1 is a material:

n is 1 or 2;

R², R³, R⁷, and R⁸ are each independently selected from optionally substituted alkyl, and optionally substituted aryl;

R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹, if present, are each members independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkanoyl, optionally substituted alkoxycarbonyl, optionally substituted alkylcarbamoyl, and a chelating ligand, wherein at least one of R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹ comprises a water soluble group:

R¹², R¹³, R¹⁴, R¹⁵, R¹⁶ R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²² and R²³ are each members independently selected from the group consisting of hydrogen, halogen, optionally substituted alkylthio, optionally substituted alkylamino and optionally substituted alkoxy, or in an alternative embodiment, at least one of i) R¹³, R¹⁴, and the carbons to which they are attached, or iii) R¹⁷, R¹⁸, and the carbons to which they are attached, or iii) R²¹, R²² and the carbons to which they are attached, join to form a fused benzene ring; and

 X^2 and X^3 are each members independently selected from the group consisting of C_1 - C_{10} alkylene optionally interrupted by a heteroatom, wherein if n is 1, the phthalocyanine may be substituted either at the 1 or 2 position and if n is 2, each R may be the same or different, or alternatively, they may join to form a 5- or 6-membered ring.

PATENT

4. (Original) The phthalocyanine dye of claim 3, wherein said dye has Formula Ia:

Ia

wherein: R², R³, R⁷, and R⁸ are each independently selected from optionally substituted alkyl, and optionally substituted aryl;

R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹, if present, are each members independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkanoyl, optionally substituted alkoxycarbonyl, optionally substituted alkylcarbamoyl, wherein at least one of R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹ comprises a water soluble group; and

R¹², R¹³, R¹⁴, R¹⁵, R¹⁶ R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²² and R²³ are each members independently selected from the group consisting of hydrogen, halogen, optionally substituted alkylthio, optionally substituted alkylamino and optionally substituted alkoxy, or in an alternative embodiment, at least one of i) R¹³, R¹⁴, and the carbons to which they are attached, or ii) R¹⁷, R¹⁸, and the carbons to which they are attached, or iii) R²¹, R²² and the carbons to which they are attached, join to form a fused benzene ring.

PATENT

5. (Currently amended) The phthalocyanine dye of claim 4, wherein L is of the formula

$$-R^1-Y-X^1-Y^1-$$

wherein

R¹ is a bivalent radical or a direct link:

Y and Y¹ are each independently selected from the group consisting of a direct link, oxygen, an optionally substituted nitrogen and sulfur; and

 X^{1} is a member selected from the group consisting of a direct link and C_{1} - C_{10} alkylene optionally interrupted by a heteroatom[[;]].

- 6. (Original) The phthalocyanine dye of claim 5, wherein R¹ is a bivalent radical selected from the group consisting of optionally substituted alkylene, optionally substituted alkyleneoxycarbonyl, optionally substituted alkylenecarbamoyl, optionally substituted alkylenesulfonylcarbamoyl, optionally substituted arylenesulfonyl, optionally substituted aryleneoxycarbonyl, optionally substituted arylenecarbamoyl, optionally substituted arylenesulfonylcarbamoyl, optionally substituted arylenesulfonylcarbamoyl, optionally substituted carboxyalkyl, optionally substituted carbamoyl, optionally substituted heteroarylene, optionally substituted heteroaryleneoxycarbonyl, optionally substituted heteroarylenecarbamoyl, optionally substituted heteroarylenecarbamoyl, optionally substituted theorems optionally substituted sulfonylcarbamoyl, optionally substituted thiocarbonyl, a optionally substituted sulfonyl, and optionally substituted sulfinyl.
- 7. (Original) The phthalocyanine dye of claim 5, wherein R², R³, R⁷, and R⁸ are each independently selected from optionally substituted alkyl, and optionally substituted aryl, R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹, if present, are each members independently selected from an optionally substituted alkyl, wherein at least two members of the group consisting of R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ comprise a water soluble functional group;

R¹², R¹³, R¹⁴, R¹⁵, R¹⁶ R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²² and R²³ are each hydrogen, halogen, optionally substituted alkylthio, optionally substituted alkylamino and optionally

PATENT

substituted alkoxy, or in an alternative embodiment, at least one of R¹³, R¹⁴, and the carbons to which they are attached, or R¹⁷, R¹⁸, and the carbons to which they are attached, or R²¹, R²² and the carbons to which they are attached, join to form a fused benzene ring;

 X^1 , X^2 and X^3 are each members independently selected from the group consisting of C_1 - C_{10} alkylene optionally interrupted by a heteroatom; and

Y and Y¹ are each independently selected from the group consisting of a direct link, oxygen, an optionally substituted nitrogen and sulfur.

8. (Original) The phthalocyanine dye of claim 7, wherein R², R³, R⁷, and R⁸ are each independently selected from optionally substituted methyl, ethyl, and isopropyl;

R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹, if present, are each members independently selected from an optionally substituted alkyl, wherein at least two members of the group consisting of R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ comprise a substituent selected from the group consisting of a carboxylate (-CO₂) group, a sulfonate (-SO₃) group, a sulfonyl (-SO₂) group, a sulfate (-SO₄-2) group, a hydroxyl (-OH) group, a phosphate (-OPO₃-2) group, a phosphonate (-PO₃-2) group, an amine (-NH₂) group and an optionally substituted quaternized nitrogen with each having an optional counter ion;

 R^{12} , R^{13} , R^{14} , R^{15} , R^{16} R^{17} , R^{18} , R^{19} , R^{20} , R^{21} , R^{22} and R^{23} are each hydrogen; X^1 , X^2 and X^3 are each members independently selected from the group

consisting of C_1 - C_{10} alkylene optionally interrupted by a heteroatom; and

Y and Y¹ are each independently selected from the group consisting of a direct link, oxygen, an optionally substituted nitrogen and sulfur.

PATENT

9. (Previously presented) The phthalocyanine dye of claim 4, wherein said dye has the formula:

wherein Q is a reactive or an activatible group selected from the group consisting of an alcohol, an activated ester, an acyl halide, an alkyl halide, an optionally substituted amine, an anhydride, a carboxylic acid, a carbodiimide, hydroxyl, iodoacetamide, an isocyanate, an isothiocyanate, a maleimide, an NHS ester, a phosphoramidite, a platinum complex, a sulfonate ester, a thiol, and a thiocyanate.

10. (Original) The phthalocyanine dye of claim 9, wherein said compound has the formula:

Ιb

Appl. No. 10/693,300 Amdt. dated June 14, 2005

Reply to Office Action of March 14, 2005

PATENT

wherein X⁴ is a C₁-C₁₀ alkylene optionally interrupted by a heteroatom.

11. (Original) The phthalocyanine dye of claim 10, wherein said compound has the formula:

Ιc

12. (Previously presented) The phthalocyanine dye of claim 4, wherein said compound has the formula:

Ιđ

PATENT

13. (Currently amended) The phthalocyanine dye of claim 4, wherein said compound has the formula:

Id-1

14. (Previously presented) The phthalocyanine dye of claim 4, wherein said compound has the formula:

PATENT

15. (Currently amended) The phthalocyavine dye of claim 4, wherein said compound has the formula:

16. (Currently amended) The phthalocyavine dye of claim 4, wherein said compound has the formula:

PATENT

 (Original) The phthalocyanine dye of claim 3, wherein said dye has the formula

If

wherein:

 Z^1 is a material;

L is a member selected from the group consisting of a direct link, or a covalent linkage, wherein said covalent linkage is linear or branched, cyclic or heterocyclic, saturated or unsaturated, having 1-60 atoms selected from the group consisting of C, N, P, O, and S, wherein L can have additional hydrogen atoms to fill valences, wherein said linkage contains any combination of ether, thioether, amine, ester, carbamate, urea, thiourea, oxy or amide bonds; or single, double, triple or aromatic carbon-carbon bonds; or phosphorus-oxygen, phosphorus-sulfur, nitrogen-nitrogen, nitrogen-oxygen, or nitrogen-platinum bonds; or aromatic or heteroaromatic bonds;

R², R³, R⁷, and R⁸ are each independently selected from optionally substituted alkyl, and optionally substituted aryl;

R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹, if present, are each members independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkanoyl, optionally substituted alkoxycarbonyl, optionally substituted alkylcarbamoyl, and a

PATENT

chelating ligand, wherein at least one of R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹ comprises a water soluble group;

R¹², R¹³, R¹⁴, R¹⁵, R¹⁶ R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²² and R²³ are each members independently selected from the group consisting of hydrogen, halogen, optionally substituted alkylthio, optionally substituted alkylamino and optionally substituted alkoxy, or in an alternative embodiment, at least one of i) R¹³, R¹⁴, and the carbons to which they are attached, or iii) R¹⁷, R¹⁸, and the carbons to which they are attached, or iii) R²¹, R²² and the carbons to which they are attached, join to form a fused benzene ring; and

 X^2 and X^3 are each members independently selected from the group consisting of C_1 - C_{10} alkylene optionally interrupted by a heteroatom.

18. (Original) The phthalocyanine dye of claim 17, wherein said material is a biomolecule;

L is of the formula:

wherein

R¹ is a bivalent radical or a direct link;

Y and Y¹ are each independently selected from the group consisting of a direct link, oxygen, an optionally substituted nitrogen and sulfur;

X¹ is a member selected from the group consisting of a direct link and C₁-C₁₀ alkylene optionally interrupted by a heteroatom:

 R^2 , R^3 , R^7 , and R^8 are each independently selected from optionally substituted alkyl, and optionally substituted aryl;

R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹, if present, are each members independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkanoyl, optionally substituted alkoxycarbonyl, optionally substituted alkylcarbamoyl, and a chelating ligand, wherein at least two of R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹ comprises a water soluble group; and

PATENT

R¹², R¹³, R¹⁴, R¹⁵, R¹⁶ R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²² and R²³ are each members independently selected from the group consisting of hydrogen, halogen, optionally substituted alkylthio, optionally substituted alkylamino and optionally substituted alkoxy, or in an alternative embodiment, at least one of i) R¹³, R¹⁴, and the carbons to which they are attached, or iii) R²¹, R²² and the carbons to which they are attached, join to form a fused benzene ring.

- 19. (Original) The phthalocyanine dye of claim 18, wherein R¹ is a bivalent radical selected from the group consisting of optionally substituted alkylene, optionally substituted alkyleneoxycarbonyl, optionally substituted alkylenecarbamoyl, optionally substituted alkylenesulfonylcarbamoyl, optionally substituted arylene, optionally substituted arylenesulfonyl, optionally substituted aryleneoxycarbonyl, optionally substituted arylenecarbamoyl, optionally substituted arylenesulfonylcarbamoyl, optionally substituted carboxyalkyl, optionally substituted carbamoyl, optionally substituted heteroarylene, optionally substituted heteroaryleneoxycarbonyl, optionally substituted heteroarylenecarbamoyl, optionally substituted heteroarylenecarbamoyl, optionally substituted heteroarylenecarbamoyl, optionally substituted thiocarbonyl, a optionally substituted sulfonylcarbamoyl, optionally substituted stituted sulfonylcarbamoyl, a optionally substituted sulfonyl, and optionally substituted sulfinyl.
- 20. (Original) The phthalocyanine dye of claim 18, wherein said biomolecule is a member selected from the group consisting of a small molecule, a marker, a cell, a liposome, a protein, a peptide, an enzyme substrate, a hormone, an antibody, an antigen, a hapten, an avidin, a streptavidin, biotin, a carbohydrate, an oligosaccharide, a polysaccharide, a nucleic acid, a deoxy nucleic acid, a fragment of DNA, a fragment of RNA, nucleotide triphosphates, acyclo terminator triphosphates, and PNA.

PATENT

21. (Currently amended) The phthalocyanine dye of claim 20, wherein said phthalocyanine dye has the formula:

22. (Currently amended) The phthalocyanine dye of claim 20, wherein said phthalocyanine dye has the formula:

23. (Original) The phthalocyanine dye of claim 20, wherein said phthalocyanine dye has the formula:

PATENT

- 24. (Original) The phthalocyanine dye of claim 18, wherein the covalent linkage between L-R¹ is selected from the group consisting of a direct bond, an amide bond, an ester bond, an ether bond, an oxime bond, a phosphate ester bond, a sulfonamide bond, a thiourea bond, and an urea bond.
- 25. (Withdrawn) A process for making a dye-labeled biomolecule, said method comprising:

contacting a biomolecule and an optional activating reagent with a compound having the formula:

Ιb

wherein:

L is a member selected from the group consisting of a direct link, or a covalent linkage, wherein said covalent linkage is linear or branched, cyclic or heterocyclic, saturated or unsaturated, having 1-60 atoms selected from the group consisting of C, N, P, O, and S, wherein L can have additional hydrogen atoms to fill valences, wherein said linkage contains any combination of ether, thioether, amine, ester, carbamate, urea, thiourea, oxy or amide bonds; or single, double, triple or aromatic carbon-carbon bonds; or phosphorus-oxygen, phosphorus-sulfur, nitrogen-nitrogen, nitrogen-oxygen, or nitrogen-platinum bonds; or aromatic or heteroaromatic bonds;

Q is a reactive or an activatible group;

PATENT

R², R³, R⁷, and R⁸ are each independently selected from optionally substituted alkyl, and optionally substituted aryl;

R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹, if present, are each members independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkanoyl, optionally substituted alkoxycarbonyl, optionally substituted alkylcarbamoyl, and a chelating ligand wherein at least one of R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹ comprises a water soluble group;

R¹², R¹³, R¹⁴, R¹⁵, R¹⁶ R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²² and R²³ are each members independently selected from the group consisting of hydrogen, halogen, optionally substituted alkylthio, optionally substituted alkylamino and optionally substituted alkoxy, or in an alternative embodiment, at least one of i) R¹³, R¹⁴, and the carbons to which they are attached, or iii) R¹⁷, R¹⁸, and the carbons to which they are attached, or iii) R²¹, R²² and the carbons to which they are attached, join to form a fused benzene ring; and

 X^2 and X^3 are each members independently selected from the group consisting of C_1 - C_{10} alkylene optionally interrupted by a heteroatom, for sufficient time, thereby making a dye-labeled biomolecule.

- 26. (Withdrawn) The process of claim 25, wherein Q is a reactive or an activatible group selected from the group consisting of an alcohol, an activated ester, an acyl halide, an alkyl halide, an optionally substituted amine, an anhydride, a carboxylic acid, a carbodiimide, hydroxyl, iodoacetamide, an isocyanate, an isothiocyanate, a maleimide, an NHS ester, a phosphoramidite, a sulfonate ester, a thiol, and a thiocyanate.
 - (Withdrawn) The process of claim 25, wherein L is of the formula:
 -R¹-Y-X¹-Y¹-

wherein

R¹ is a bivalent radical or a direct link;

Y and Y¹ are each independently selected from the group consisting of a direct link, oxygen, an optionally substituted nitrogen and sulfur;

PATENT

 X^{l} is a member selected from the group consisting of a direct link and C_{l} - C_{l0} alkylene optionally interrupted by a heteroatom;

R², R³, R⁷, and R⁸ are each independently selected from optionally substituted alkyl, and optionally substituted aryl;

R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹, if present, are each members independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkanoyl, optionally substituted alkoxycarbonyl, optionally substituted alkylcarbamoyl, and a chelating ligand, wherein at least two of R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹ comprises a water soluble group; and

R¹², R¹³, R¹⁴, R¹⁵, R¹⁶ R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²² and R²³ are each members independently selected from the group consisting of hydrogen, halogen, optionally substituted alkylthio, optionally substituted alkylamino and optionally substituted alkoxy, or in an alternative embodiment, at least one of i) R¹³, R¹⁴, and the carbons to which they are attached, or iii) R¹⁷, R¹⁸, and the carbons to which they are attached, or iii) R²¹, R²² and the carbons to which they are attached, join to form a fused benzene ring.

- 28. (Withdrawn) The process of claim 25, wherein R¹ is a bivalent radical selected from the group consisting of optionally substituted alkylene, optionally substituted alkyleneoxycarbonyl, optionally substituted alkylenecarbamoyl, optionally substituted alkylenesulfonylcarbamoyl, optionally substituted arylene, optionally substituted arylenesulfonyl, optionally substituted aryleneoxycarbonyl, optionally substituted arylenecarbamoyl, optionally substituted arylenesulfonylcarbamoyl, optionally substituted carboxyalkyl, optionally substituted carbamoyl, optionally substituted carboxyalkyl, optionally substituted heteroarylene, optionally substituted heteroaryleneoxycarbonyl, optionally substituted heteroarylenecarbamoyl, optionally substituted heteroarylenecarbamoyl, optionally substituted heteroarylenesulfonylcarbamoyl, optionally substituted sulfonylcarbamoyl, optionally substituted thiocarbonyl, a optionally substituted sulfonyl, and optionally substituted sulfinyl.
- 29. (Currently amended) The process of claim 25, wherein R², R³, R⁷, and R⁸ are each independently selected from optionally substituted alkyl, and optionally substituted aryl;

PATENT

R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹, if present, are each members independently selected from an optionally substituted alkyl, wherein at least two members of the group consisting of R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ comprise a water soluble functional group;

R¹², R¹³, R¹⁴, R¹⁵, R¹⁶ R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²² and R²³ are each hydrogen, halogen, optionally substituted alkylthio, optionally substituted alkylamino and optionally substituted alkoxy, or in an alternative embodiment, at least one of R¹³, R¹⁴, and the carbons to which they are attached, or R¹⁷, R¹⁸, and the carbons to which they are attached, or R²¹, R²² and the carbons to which they are attached, join to form a fused benzene ring;

 X^1 , X^2 and X^3 are each members independently selected from the group consisting of C_1 - C_{10} alkylene optionally interrupted by a heteroatom; and

Y and Y¹ are each independently selected from the group consisting of a direct link, oxygen, an optionally substituted nitrogen and sulfur[[;]].

30. (Currently amended) The process of claim 25, wherein R², R³, R⁷, and R⁸ are each independently selected from optionally substituted methyl, ethyl, and isopropyl;

R⁴, R⁵, R⁶, R⁹, R¹⁰, and R¹¹, if present, are each members independently selected from an optionally substituted alkyl, wherein at least two members of the group consisting of R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ comprise a substituent selected from the group consisting of a carboxylate (-CO₂) group, a sulfonate (-SO₃) group, a sulfonyl (-SO₂) group, a sulfate (-SO₄-2) group, a hydroxyl (-OH) group, a phosphate (-OPO₃-2) group, a phosphonate (-PO₃-2) group, an amine (-NH₂) group and an optionally substituted quaternized nitrogen with each having an optional counter ion;

R¹², R¹³, R¹⁴, R¹⁵, R¹⁶ R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²² and R²³ are each hydrogen;

 X^1 , X^2 and X^3 are each members independently selected from the group consisting of C_1 - C_{10} alkylene optionally interrupted by a heteroatom; and

Y and Y¹ are each independently selected from the group consisting of a direct link, oxygen, an optionally substituted nitrogen and sulfur[[;]].

31. (Withdrawn) The process of claim 25, wherein said compound has the formula:

PATENT

Ic

wherein X^4 is a $C_1\text{-}C_{10}$ alkylene optionally interrupted by a heteroatom.

32. (Withdrawn) The process of claim 25, wherein said compound has the formula:

Id

33. (Currently amended) The process of claim 25, wherein said compound has the formula:

PATENT

Id-1 .

34. (Currently amended) The process of claim 25, wherein said compound has the formula:

Ιe .

35. (Currently amended) The process of claim 25, wherein said compound has the formula:

<u>PATENT</u>

Ie-1 .

36. (Withdrawn) The process of claim 25, wherein said compound has the formula:

- 37. (Withdrawn) A kit for labeling a biomolecule, said kit comprising: a compound according to claim 1; and instructions for use.
- 38. (Withdrawn) The kit of claim 37, wherein said kit further comprises a buffer.